



A31304 B-A-B 069906.0132
PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Mitchell *et al.*
Serial No. : 09/756,096 Examiner : Epps Ford, Janet L
Filed : January 8, 2001 Group Art Unit: 1638
For : METHODS AND COMPOSITIONS FOR USE IN SPLICEOSOME
MEDIATED RNA TRANS-SPLICING

INFORMATION DISCLOSURE STATEMENT

I hereby certify that this paper is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, Box 1450, Alexandria, VA 22313-1450.

March 19, 2004

Carmella L. Stephens
Attorney Name

Carmella L. Stephens
Signature

41,328
PTO Registration No

March 19, 2004
Date of Signature

Commissioner for Patents
Box 1450
Alexandria, VA 22313-1450

Sir:

Pursuant to 37 C.F.R. §§1.97 and 1.98, applicants respectfully request that the documents listed below in reverse chronological order and on the accompanying PTO 1449 be considered by the Examiner and made of record in the above-referenced application. Copies of the documents listed are enclosed.

1. United States Patent Application Serial No. 10/434,727, filed May 8, 2003, "Use of spliceosome-mediated RNA trans-splicing to confer cell selective replication to adenoviruses," Otto, E.
2. United States Patent Application Serial No. 10/374,784, filed February 25, 2003, "Trans-splicing mediated imaging of gene expression," Mitchell et al.
3. United States Patent Application Serial No. 10/198,447, filed July 17, 2002, "Spliceosome mediated RNA trans-splicing for correction of skin disorders," Mitchell et al.
4. United States Patent Application Serial No. 10/136,723, filed April 30, 2002, "Transgenic Animal Model for Spliceosome-mediated RNA trans-splicing," Puttaraju et al.
5. United States Patent Application Serial No. 10/103,294, filed March 30, 2002, "Spliceosome mediated RNA trans-splicing," Mitchell et al.
6. United States Patent Application Serial No. 10/075,028, filed March 12, 2002, "Method and compositions for use in spliceosome mediated RNA trans-splicing," Mitchell et al.
7. United States Patent Application Serial No. 10/076,248, filed February 12, 2002, "Method and compositions for use in spliceosome mediated RNA trans-splicing," Mitchell et al.
8. United States Patent Application Serial No. 10/941,492, filed August 29, 2001, "Method and compositions for use in spliceosome mediated RNA trans-splicing," Mitchell et al.
9. United States Patent Application Serial No. 09/838,858, filed April 20, 2001, "Method and compositions for use in spliceosome mediated RNA trans-splicing," Mitchell et al.
10. United States Patent Application Serial No. 09/756,095, filed Jan. 8, 2001, published August 22, 2002, as U.S. Patent Publication No. US20020115207, "Method and compositions for use on spliceosome mediated RNA trans-splicing," Mitchell et al.

11. United States Patent No. 6,280,978, filed Sept. 23, 1998, issued August 28, 2001, "Method and compositions for use in spliceosome mediated RNA trans-splicing," Mitchell et al.
12. United States Patent Application Serial No. 09/756,097, filed Jan. 8, 2001, "Method and compositions for use in spliceosome mediated RNA trans-splicing in plants," Mitchell et al.
13. United States Patent No. 6,083,702, filed Aug. 13, 1998, issued July 4, 2000, "Method and compositions for use in spliceosome mediated RNA trans-splicing," Mitchell et al.
14. United States Patent No. 6,013,487, filed Dec. 13, 1996, issued Jan. 11, 2000, "Chimeric RNA molecules generated by trans-splicing," of Lloyd Mitchell.
15. Mansfield et al., 2000, "Repair of CFTR mRNA by spliceosome-mediated RNA trans-splicing," *Gene Therapy* 7:1885-1895.
16. Lan N *et al.*, 1998, "Ribozyme-mediated Repair of Sickle β -Globin mRNAs in Erythrocyte Precursors" *Science* 280:1593-1596.
17. Phylactou LA *et al.*, 1998, "Ribozyme-mediated trans-splicing of a trinucleotide repeat" *Nature Genetics* 18:378-381.
18. Staley JP *et al.*, 1998, "Mechanical Devices of the Spliceosome: Motors, Clocks, Springs and Things" *Cell* 92:315-326.
19. Bellet et al., 1997, "Malignant transformation of nontrophoblastic cells is associated with the expression of chorionic gonadotropin β genes normally transcribed in trophoblastic cells," *Cancer Res.* 57:516.
20. Coolidge et al., 1997, "Functional analysis of the polypyrimidine tract in pre-mRNA splicing," *Nucleic Acids Res.* 25:888.

21. Malek O *et al.*, 1997, "Evolution of trans-splicing plant mitochondrial introns in pre-Permian times" *Proc. Nat'l. Acad. Sci. USA* 94:553-558.
22. Hoon *et al.*, 1996, "Detection of metastatic breast cancer by β -hCG polymerase chain reaction," *Int J. Cancer* 69:369.
23. Jones JT *et al.*, 1996, "Tagging ribozyme reaction sites to follow trans-splicing in mammalian cells" *Nature Medicine* 2:643-648.
24. Krämer A, 1996, "The structure and function of proteins involved in mammalian Pre-mRNA splicing" *Annu. Rev. Biochem.* 65:367-404.
25. Nisson, 1996, "Multiple affinity domains for the detection, purification, and immobilization of recombinant proteins," *J. et al. J. Mol. Recognit.*, 1996, 5:585-594.
26. Pasman Z *et al.*, 1996, "The 5' and 3' splice sites come together via a three dimensional diffusion mechanism" *Nucleic Acids Res.* 24(9):1638-1645.
27. Bruzik JP *et al.*, 1995, "Enhancer-dependent interaction between 5' and 3' splice sites in trans" *Proc. Nat'l. Acad. Sci. USA* 92:7056-7059.
28. Chiara MD *et al.*, 1995, A two-step mechanism for 5' and 3' splice-site pairing" *Nature* 375:510-513.
29. Davis RE *et al.*, 1995, "RNA Trans-splicing in Flatworms" *J. Biol. Chem.* 270:21813-21819.
30. Eul J *et al.*, 1995, "Experimental evidence for RNA trans-splicing in mammalian cells: *EMBO. J.* 14(13):3226-3235.
31. Hollenberg *et al.*, 1994, "Multiple promoter elements in the human chorionic gonadotropin b subunit genes distinguish their expression from luteinizing hormone β gene," *Mol. Cell Endo.*, 106:111-119.

32. Sullenger BA *et al.*, 1994, "Ribozyme-mediated repair of defective mRNA by targeted trans-splicing" *Nature* 341:619-622.
33. Goldspiel et al., 1993, "Human gene therapy," *Clinical Pharmacy* 12:488-505.
34. Kozarsky and Wilson, 1993, "Gene therapy:adenovirus vectors," *Current Opinion in Genetics and Development* 3:499-503.
35. Miller *et al.*, 1993, "Use of adenoviral vectors for gene transfer and expression," *Meth. Enzymol.* 217:581-599.
36. Moore and Sharp, 1993, "Evidence for two active sites in the spliceosome provided by stereochemistry of pre-mRNA splicing," *Nature*, 365:364-368.
37. Moore, 1993, "Splicing of precursors to mRNA by the spliceosome," in *RNA World*, R.F. Gesteland and J.F. Atkins, eds. Cold Spring Harbor Laboratory Press, p303-358.
38. Morgan and Anderson, 1993, "Human Gene Therapy," *Ann. Rev. Biochem.* 62:191-217.
39. Mulligan, 1993, "The basic science of gene therapy," *Science* 260:926-932.
40. Roscigno et al., 1993, "A mutational analysis of the polypyrimidine tract of introns," *J. Bio. Chem.*, 268:11222-11229.
41. Tolstoshev, 1993, "Gene therapy, concepts, current trials, and future directions," *Ann. Rev. Pharmacol. Toxicol.* 33:573-596.
42. Acevedo et al., 1992, "Human chorionic gonadotropin-beta subunit gene expression in cultured human fetal and cancer cells of different types and origins," *Cancer* 76:1467.
43. Bruzik JP *et al.*, 1992, "Spliced leader RNAs from lower eukaryotes are trans-spliced in mammalian cells: *Nature* 360:692-695.

44. Vellard M *et al.*, 1992, "A potential splicing factor is encoded by the opposite strand of the trans-spliced *c-myb* exon" *Proc. Nat'l. Acad. Sci.*, 89:2511-2515.
45. Janknecht et al., 1991, "Rapid and efficient purification of native histidine-tagged protein expressed by recombinant vaccinia virus," *Proc. Natl. Acad. Sci.*, 88:8972-8976.
46. Wu and Wu, 1991, "Delivery systems for gene therapy," *Biotherapy* 3:87-95
47. United States Patent No. 4,980,286, issued Dec. 25, 1990 of Morgan et al.
48. Rajkovic A *et al.*, 1990, "A spliced leader is present on a subset of mRNAs from the human parasite *Schistosoma mansoni*" *Proc. Nat'l. Acad. Sci. USA*, 87:8879-8883.
49. Schneider et al., 1990, "Building blocks for oligonucleotide analogs with dimethyl-sulfide-sulfoxide and sulfone groups replacing phosphodiester linkages," *Tet. Letters*, 31:335.
50. Senapathy et al., 1990, "Splice junctions, branch point sites, and exons:sequence statistics, identification, and applications to genome project," *Methods of Enzymology*, 183:252-278.
51. Uhlmann et al., 1990, "Antisense oligonucleotides:a new therapeutic principle," *Chem Rev.*, 90:543-549.
52. International Patent Application No. PCT/US89/01589 of , published on November 2, 1989 as International Publication No. WO89/10134.
53. Kerem et al., 1989, "Identification of the Cystic Fibrosis Gene:Genetic analysis," *Science*, 245:1073-1080.
54. Letsinger et al., 1989, "Cholesterol-conjugated oligonucleotides;synthesis, properties, and activity as inhibitors of replication of human immunodeficiency virus in cell culture, " *Proc. Natl. Acad. Sci.*, 86:6553-6556

55. Reed, 1989, "The organization of 3' splice sites sequences in mammalian introns," *Genes Dev.* 3:2113.
56. Riordan et al., 1989, "Identification of the Cystic Fibrosis Gene: Cloning and characterization of complementary DNA," *Science*, 245:1066-1073.
57. Rommens et al., 1989, "Identification of the Cystic Fibrosis Gene: Chromosome walking and jumping," *Science*, 245:1059-1065.
58. Shimizu A *et al.*, 1989, "Immunoglobulin double-isotype expression by trans-mRNA in a human immunoglobulin transgenic mouse" *Proc. Nat'l. Acad. Sci. USA* 86:8020-8023.
59. Smith et al., 1989, "Scanning from an independently specified branch point defines the 3' splice site of mammalian introns," *Nature*, 342-243-247.
60. International Patent Application No. PCT/US88/02009 of Synthetic Genetics, published on Dec. 15, 1988 as International Publication No. WO88/09810.
61. van der Krol et al., 1988, "Modulation of eukaryotic gene expression by complementary RNA or DNA sequences," *BioTechniques*, 6:958-976.
62. Reed & Maniatis 1988, "The role of the mammalian branchpoint sequence in the pre-mRNA splicing," *Genes Dev.* 2:1268.
63. Smith et al, 1988, "Single-step purification of polypeptides expressed in *Escherichia coli* as fusions with glutathione S-transferase," *Gene*, 67:31
64. Zon et al., 1988, "Oligonucleotide analogues as potential chemotherapeutic agents," *Pharm. Res.*, 5:539-549.
65. Krause M *et al.*, 1987, "A Trans-spliced Leader Sequence on Actin mRNA in *C. elegans*" *Cell* 49:753-761.

66. Lemaitre et al., 1987, "Specific antiviral activity of a poly(L-lysine)-conjugated oligodeoxyribonucleotide sequence complementary to vesicular stomatitis virus N protein mRNA initiation site," *Proc. Natl. Acad. Sci.*, 84:648-652.
67. Wu and Wu, 1987, "Receptor-mediated in vitro gene transformation by a soluble DNA carrier system," *J. Biol. Chem.*, 262:429-4432.
68. Murphy et al., 1986, "Identification of a novel Y branch structure as an intermediate in Trypanosome mRNA processing:evidence for Trans splicing," *Cell*, 47:517.
69. Smith et al., 1986, "Mr 26,000 antigen of *Schistosoma japonica* recognized by resistant WEH1 129/J mice is a parasite glutathione S-transferase," *Proc. Natl. Acad. Sci.*, 83:8703-8707.
70. Sutton RE *et al.*, 1986, "Evidence for Trans Splicing in Trypanosomes" *Cell* 47:527-535.
71. Konarska MM *et al.*, 1985, "Trans Splicing of mRNA Precursors In Vitro" *Cell* 46:165-171.
72. Solnick D, 1985, "Trans Splicing of mRNA Precursors" *Cell* 42:157-164.
73. Talmadge et al., 1984, "Only three of the seven chorionic gonadotropin beta subunit genes can be expressed in the placenta," *Nucleic Acids Res.* 12:8415.
74. Accession No. K01722, *Corynebacteriophage beta diphtheria toxin (DT) gene*, 1983.
75. Greenfield, 1983, "Nucleotide sequence of the structural gene for the diphtheria toxin carried by corynebacteriophage β ," *Proc. Natl. Acad. Sci.*, 80:6853-6857.
76. Brinster et al., 1982, "Regulation of metallothionein-thymidine kinase fusion plasmids injected into mouse eggs," *Nature*, 296:39-42.

77. Benoist et al., 1981, ""In vivo sequence requirements of the SV40 early promoter region," *Nature*, 290:304-310.
78. Wagner TE *et al.*, 1981, "Microinjection of a rabbit β -globin gene into zygotes and its subsequent expression in adult mice and their offspring" *Proc. Natl. Acad. Sci. USA* 78(10):6376-6380.
79. Yamamoto et al., 1980, "Identification of a functional promoter in the long terminal repeat of Rous Sarcoma Virus," *Cell*, 22:39-42.
80. Berget SM *et al.*, 1977, "Spliced segments at the 5' terminus of adenovirus 2 late mRNA" *Proc. Natl. Acad. Sci. USA* 74(8):3171-3175.
81. Chow LT *et al.*, 1977, "An Amazing Sequence Arrangement at the 5' Ends of Adenovirus 2 Messenger RNA" *Cell* 12:1-8.
82. Uchida et al, 1973, "Diphtheria toxin and related proteins: isolation and properties of mutant proteins related to diphtheria toxin," *J. Biol. Chem.*, 248:3838.

References #1-10, and 12 are related co-pending U.S. patent application.

Identification of the above-listed citations is not to be construed as an admission of the applicants or attorneys for applicants that such citations are available as "prior art" against the subject application.

Pursuant to 37 C.F.R. § 1.97(b)(3), this Information Disclosure Statement is being filed, the applicants believe, before the mailing date of a first Office Action on the merits. Thus, there should be no fee required for this submission. However, if any fee is required, or if any overpayment has been made, the Commissioner is hereby authorized to charge any fees, or credit or any overpayments made, to Deposit Account 02-4377. A duplicate copy of this paper is enclosed.

Respectfully submitted,
BAKER BOTTS L.L.P.

By: *Carmella L. Stephens*
Rochelle K. Seide
Patent Office Reg. No. 32,300

Carmella L. Stephens
Patent Office Reg. No. 41,328

30 Rockefeller Plaza
44th Floor
New York, NY 10112
(212) 408-2500

Attorneys for Applicants

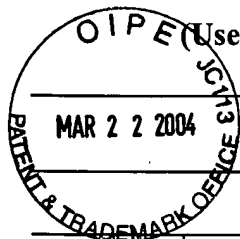
**INFORMATION DISCLOSURE STATEMENT
BY APPLICANT**

(Use several sheets if necessary)

Applicant
Mitchell et al.

Filing Date
Jan. 8, 2001

Group



U.S. PATENT DOCUMENTS

*Exam. Init.	Document No.	Date	Name	Class	Subclass	Filing Date if Appropriate
11	6 2 8 0 9 7 8	8/28/01	Mitchell et al.	435	91.3	
13	6 0 8 3 7 0 2	7/4/00	Mitchell et al.	435	6	
14	6 0 1 3 4 8 7	1/11/00	Mitchell et al.	435	91.3	
47	4 9 8 0 2 8 6	12/25/90	Morgan et al.	435	172..3	

FOREIGN PATENT DOCUMENT

Document No.	Date	Country	Class	SubClass	Translation Yes No
52 8 9 1 0 1 3 4	11/2/89	WIPO			
60 8 8 0 9 8 1 0	12/15/88	WIPO			

OTHER DOCUMENTS (including Author, Title Date, Pertinent Pages, Etc.)

1	United States Patent Application Serial No. 10/434,727, filed May 8, 2003, "Use of spliceosome-mediated RNA trans-splicing to confer cell selective replication to adenoviruses," Otto, E.
2	United States Patent Application Serial No. 10/374,784, filed February 25, 2003, "Trans-splicing mediated imaging of gene expression," Mitchell et al.
3	United States Patent Application Serial No. 10/198,447, filed July 17, 2002, "Spliceosome mediated RNA trans-splicing for correction of skin disorders," Mitchell et al.
4	United States Patent Application Serial No. 10/136,723, filed April 30, 2002, "Transgenic Animal Model for Spliceosome-mediated RNA trans-splicing," Puttaraju et al.

NY02:452500.1

1

Examiner

Date Considered

* Examiner: Initial citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

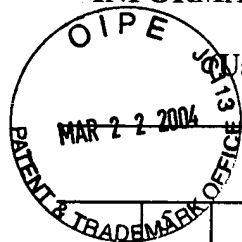
**INFORMATION DISCLOSURE STATEMENT
BY APPLICANT**

(Use several sheets if necessary)

Applicant
Mitchell et al.

Filing Date
Jan. 8, 2001

Group



		United States Patent Application Serial No. 10/103,294, filed March 30, 2002, "Spliceosome mediated RNA trans-splicing," Mitchell et al.
6		United States Patent Application Serial No. 10/075,028, filed March 12, 2002, "Method and compositions for use in spliceosome mediated RNA trans-splicing," Mitchell et al.
7		United States Patent Application Serial No. 10/076,248, filed February 12, 2002, "Method and compositions for use in spliceosome mediated RNA trans-splicing," Mitchell et al.
8		United States Patent Application Serial No. 10/941,492, filed August 29, 2001, "Method and compositions for use in spliceosome mediated RNA trans-splicing," Mitchell et al.
9		United States Patent Application Serial No. 09/838,858, filed April 20, 2001, "Method and compositions for use in spliceosome mediated RNA trans-splicing," Mitchell et al.
10		United States Patent Application Serial No. 09/756,095, filed Jan. 8, 2001, published August 22, 2002, as U.S. Patent Publication No. US20020115207, "Method and compositions for use on spliceosome mediated RNA trans-splicing," Mitchell et al.
12		United States Patent Application Serial No. 09/756,097, filed Jan. 8, 2001, "Method and compositions for use in spliceosome mediated RNA trans-splicing in plants," Mitchell et al.
15		Mansfield et al., 2000, "Repair of CFTR mRNA by spliceosome-mediated RNA trans-splicing," <i>Gene Therapy</i> 7:1885-1895.
16		Lan N <i>et al.</i> , 1998, "Ribozyme-mediated repair of Sickle β -Globin mRNAs in Erythrocyte Precursors" <i>Science</i> 280:1593-1596.
17		Phylactou LA <i>et al.</i> , 1998, "Ribozyme-mediated trans-splicing of a trinucleotide repeat" <i>Nature Genetics</i> 18:378-381.
18		Staley JP <i>et al.</i> , 1998, "Mechanical Devices of the Spliceosome: Motors, Clocks, Springs and Things" <i>Cel</i> 92:315-326.

NY02:452500.1

Examiner

Date Considered

* Examiner: Initial citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

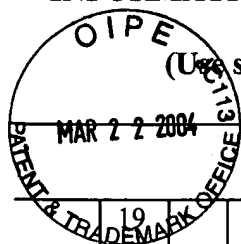
**INFORMATION DISCLOSURE STATEMENT
BY APPLICANT**

(Use several sheets if necessary)

Applicant
Mitchell et al.

Filing Date
Jan. 8, 2001

Group



19	Bellet et al., 1997, "Malignant transformation of nontrophoblastic cells is associated with the expression of chorionic gonadotropin β genes normally transcribed in trophoblastic cells," <i>Cancer Res.</i> 57:516.
20	Coolidge et al., 1997, "Functional analysis of the polypyrimidine tract in pre-mRNA splicing," <i>Nucleic Acids Res.</i> 25:888.
21	Malek O et al., 1997, "Evolution of trans-splicing plant mitochondrial introns in pre-Permian times" <i>Proc. Nat'l. Acad. Sci. USA</i> 94:553-558.
22	Hoon et al., 1996, "Detection of metastatic breast cancer by β -hCG polymerase chain reaction," <i>Int J. Cancer</i> 69:369.
23	Jones JT et al., 1996, "Tagging ribozyme reaction sites to follow trans-splicing in mammalian cells" <i>Nature Medicine</i> 2:643-648.
24	Krämer A, 1996, "The structure and function of proteins involved in mammalian Pre-mRNA splicing" <i>Annu. Rev. Biochem.</i> 65:367-404.
25	Nisson, 1996, "Multiple affinity domains for the detection, purification, and immobilization of recombinant proteins," J. et al. <i>J. Mol. Recognit.</i> , 1996, 5:585-594.
26	Pasman Z et al., 1996, "The 5' and 3' splice sites come together via a three dimensional diffusion mechanism" <i>Nucleic Acids Res.</i> 24(9):1638-1645.
27	Bruzik JP et al., 1995, "Enhancer-dependent interaction between 5' and 3' splice sites in trans" <i>Proc. Nat'l Acad. Sci. USA</i> 92:7056-7059.
28	Chiara MD et al., 1995, "A two-step mechanism for 5' and 3' splice-site pairing" <i>Nature</i> 375:510-513.
29	Davis RE et al., 1995, "RNA Trans-splicing in Flatworms" <i>J. Biol. Chem.</i> 270:21813-21819.
30	Eul J et al., 1995, "Experimental evidence for RNA trans-splicing in mammalian cells: <i>EMBO. J.</i> 14(13):3226-3235.

NY02:452500.1

Examiner

Date Considered

* Examiner: Initial citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Applicant
Mitchell et al.

Filing Date
Jan. 8, 2001

Group

**INFORMATION DISCLOSURE STATEMENT
BY APPLICANT**

(Use several sheets if necessary)

MAR 22 2004

31		Hollenberg et al., 1994, "Multiple promoter elements in the human chorionic gonadotropin b subunit genes distinguish their expression from luteinizing hormone β gene," Mol. Cell Endo., 106:111-119.
32		Sullenger BA <i>et al.</i> , 1994, "Ribozyme-mediated repair of defective mRNA by targeted trans-splicing" <i>Nature</i> 341:619-622.
33		Goldspiel et al., 1993, "Human gene therapy," Clinical Pharmacy 12:488-505.
34		Kozarsky and Wilson, 1993, "Gene therapy:adenovirus vectors," Current Opinion in Genetics and Development 3:499-503.
35		Miller <i>et al.</i> , 1993, "Use of adenoviral vectors for gene transfer and expression," Meth. Enzymol. 217:581-599.
36		Moore and Sharp, 1993, "Evidence for two active sites in the spliceosome provided by stereochemistry of pre mRNA splicing," Nature, 365:364-368.
37		Moore, 1993, "Splicing of precursors to mRNA by the spliceosome," in RNA World, R.F. Gesteland and J.F. Atkins, eds. Cold Spring Harbor Laboratory Press, p303-358.
38		Morgan and Anderson, 1993, "Human Gene Therapy," Ann. Rev. Biochem. 62:191-217.
39		Mulligan, 1993, "The basic science of gene therapy," Science 260:926-932.
40		Roscigno et al., 1993, "A mutational analysis of the polypyrimidine tract of introns," J. Bio. Chem., 268:11222-11229.
41		Tolstoshev, 1993, "Gene therapy, concepts, current trials, and future directions," Ann. Rev. Pharmacol. Toxicol. 33:573-596.
42		Acevedo et al., 1992, "Human chorionic gonadotropin-beta subunit gene expression in cultured human feta and cancer cells of different types and origins," Cancer 76:1467.

NY02:452500.1

4

Examiner

Date Considered

* Examiner: Initial citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

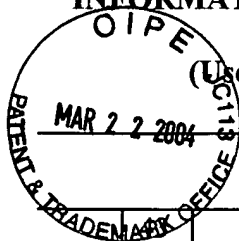
Applicant
Mitchell et al.

Filing Date
Jan. 8, 2001

Group

**INFORMATION DISCLOSURE STATEMENT
BY APPLICANT**

(Use several sheets if necessary)



Bruzik JP *et al.*, 1992, "Spliced leader RNAs from lower eukaryotes are trans-spliced in mammalian cells: *Nature* 360:692-695.

44 Vellard M *et al.*, 1992, "A potential splicing factor is encoded by the opposite strand of the trans-spliced *c-myc* exon" *Proc. Nat'l. Acad. Sci.*, 89:2511-2515.

45 Janknecht *et al.*, 1991, "Rapid and efficient purification of native histidine-tagged protein expressed by recombinant vaccinia virus," *Proc. Natl. Acad. Sci.*, 88:8972-8976.

46 Wu and Wu, 1991, "Delivery systems for gene therapy," *Biotherapy* 3:87-95. 4,980,286, issued Dec. 25, 1990 of Morgan *et al.*

48 Rajkovic A *et al.*, 1990, "A spliced leader is present on a subset of mRNAs from the human parasite *Schistosoma mansoni*" *Proc. Nat'l. Acad. Sci. USA*, 87:8879-8883.

49 Schneider *et al.*, 1990, "Building blocks for oligonucleotide analogs with dimethyl-sulfide-sulfoxide and sulfone groups replacing phosphodiester linkages," *Tet. Letters*, 31:335.

50 Senapathy *et al.*, 1990, "Splice junctions, branch point sites, and exons: sequence statistics, identification, and applications to genome project," *Methods of Enzymology*, 183:252-278.

51 Uhlmann *et al.*, 1990, "Antisense oligonucleotides: a new therapeutic principle," *Chem Rev.*, 90:543-549.

53 Kerem *et al.*, 1989, "Identification of the Cystic Fibrosis Gene: Genetic analysis," *Science*, 245:1073-1080.

54 Letsinger *et al.*, 1989, "Cholesterol-conjugated oligonucleotides; synthesis, properties, and activity as inhibitors of replication of human immunodeficiency virus in cell culture," *Proc. Natl. Acad. Sci.*, 86:6553-6556

55 Reed, 1989, "The organization of 3' splice sites sequences in mammalian introns," *Genes Dev.* 3:2113.

56 Riordan *et al.*, 1989, "Identification of the Cystic Fibrosis Gene: Cloning and characterization of complementary DNA," *Science*, 245:1066-1073.

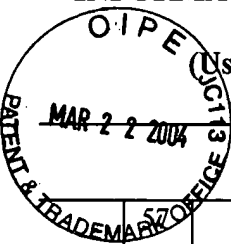
**INFORMATION DISCLOSURE STATEMENT
BY APPLICANT**

(Use several sheets if necessary)

Applicant
Mitchell et al.

Filing Date
Jan. 8, 2001

Group



		Rommens et al., 1989, "Identification of the Cystic Fibrosis Gene: Chromosome walking and jumping," Science, 245:1059-1065.
58		Shimizu A <i>et al.</i> , 1989, "Immunoglobulin double-isotype expression by trans-mRNA in a human immunoglobulin transgenic mouse" <i>Proc. Nat'l. Acad. Sci. USA</i> 86:8020-8023.
59		Smith et al., 1989, "Scannine from an independently specified branch point defines the 3' splice site of mammalian introns," <i>Nature</i> , 342-243-247.
61		van der Krol et al., 1988, "Modulation of eukaryotic gene expression by complementary RNA or DNA sequences," <i>BioTechniques</i> , 6:958-976.
62		Reed & Maniatis 1988, "The role of the mammalian branchpoint sequence in the pre-mRNA splicing," <i>Genes Dev.</i> 2:1268.
63		Smith et al, 1988, "Single-step purification of polypeptides expressed in <i>Escherichia coli</i> as fusions with glutathione S-transferase," <i>Gene</i> , 67:31
64		Zon et al., 1988, "Oligonucleotide analogues as potential chemotherapeutic agents," <i>Pharm. Res.</i> , 5:539-549.
65		Krause M <i>et al.</i> , 1987, "A Trans-spliced Leader Sequence on Actin mRNA in <i>C. elegans</i> " <i>Cell</i> 49:753-761
66		Lemaitre et al., 1987, "Specific antiviral activity of a poly(L-lysine)-conjugated oligodeoxyribonucleotide sequence complementary to vesicular stomatitis virus N protein mRNA initiation site," <i>Proc. Natl. Acad. Sci.</i> , 84:648-652.
67		Wu and Wu, 1987, "Receptor-mediated in vitro gene transformation by a soluble DNA carrier system," <i>J. Biol. Chem.</i> , 262:429-4432.
68		Murphy et al., 1986, "Identification of a novel Y branch structure as an intermediate in Trypanosome m RNA processing:evidence for Trans splicing," <i>Cell</i> , 47:517.
69		Smith et al., 1986, "Mr 26,000 antigen of <i>Schistosoma japonica</i> recognized by resistant WEH1 129/J mice is a parasite glutathione S-transferase," <i>Proc. Natl. Acad. Sci.</i> , 83:8703-8707.

NY02:452500.1

Examiner

Date Considered

* Examiner: Initial citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

**INFORMATION DISCLOSURE STATEMENT
BY APPLICANT**

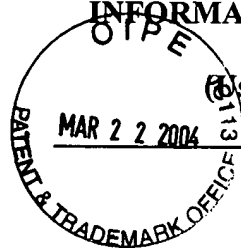
(Use several sheets if necessary)

Applicant
Mitchell et al.

Filing Date
Jan. 8, 2001

Group

MAR 22 2004



70		Sutton RE <i>et al.</i> , 1986, "Evidence for Trans Splicing in Trypanosomes" <i>Cell</i> 47:527-535.
71		Konarska MM <i>et al.</i> , 1985, "Trans Splicing of mRNA Precursors In Vitro" <i>Cell</i> 46:165-171.
72		Solnick D, 1985, "Trans Splicing of mRNA Precursors" <i>Cell</i> 42:157-164.
73		Talmadge <i>et al.</i> , 1984, "Only three of the seven chorionic gonadotropin beta subunit genes can be expressed in the placenta," <i>Nucleic Acids Res.</i> 12:8415.
74		Accession No. K01722, Corynebacteriophage beta diphtheria toxin (DT) gene, 1983.
75		Greenfield, 1983, "Nucleotide sequence of the structural gene for the diphtheria toxin carried by corynebacteriophage β ," <i>Proc. Natl. Acad. Sci.</i> , 80:6853-6857.
76		Brinster <i>et al.</i> , 1982, "Regulation of metallothionein-thymidine kinase fusion plasmids injected into mouse eggs," <i>Nature</i> , 296:39-42.
77		Benoist <i>et al.</i> , 1981, "In vivo sequence requirements of the SV40 early promoter region," <i>Nature</i> , 290:304-310.
78		Wagner TE <i>et al.</i> , 1981, "Microinjection of a rabbit β -globin gene into zygotes and its subsequent expression in adult mice and their offspring" <i>Proc. Natl. Acad. Sci. USA</i> 78(10):6376-6380.
79		Yamamoto <i>et al.</i> , 1980, "Identification of a functional promoter in the long terminal repeat of Rous Sarcoma Virus," <i>Cell</i> , 22:39-42.
80		Berget SM <i>et al.</i> , 1977, "Spliced segments at the 5' terminus of adenovirus 2 late mRNA" <i>Proc. Natl. Acad. Sci. USA</i> 74(8):3171-3175.

NY02:452500.1

7

Examiner

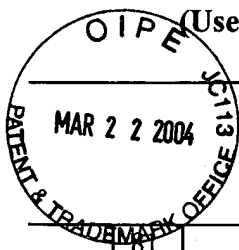
Date Considered

* Examiner: Initial citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Applicant
Mitchell et al.

Filing Date
Jan. 8, 2001

Group

[illegible]

Date Considered

* Examiner: Initial citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.